

REMARKS

Upon entry of the present amendments, claims 14-39 are pending. Claims 14, 21, 24-27, 34, and 37-39 are amended herein. The foregoing amendment is made without any intention to abandon the subject matter of the claims as filed September 17, 2003, but the intention that claims of the same, lesser or greater scope may be pursued in the present application or in a continuation, continuation-in-part, or divisional application. Applicant believes that the present amendment does not add new matter.

Support for the claim amendments can be found in the claims and the specification, as follows:

Claims 14 and 21 are amended to correct the antecedent basis of the term "mammal." Claims 14, 21, 27, and 34 are further amended to clarify that it is the antioxidants that are required to be amphipathic rather than the liposomes. Support for these amendments can be found in, *e.g.*, Specification page 7, line 6 through page 9, line 2; page 19, lines 8-25; and FIG. 8. Claims 24-27, 34, and 37-39 are amended to correct a grammatical errors. Claims 21, 24-27, 34, and 37-39 are further amended to add an antioxidant that was inadvertently omitted from the Markush group in some of the claims. Support for these amendments can be found in, *e.g.*, previously presented claims 15 and 28; as well as Specification page 17, line 24 through page 18, line 10. Claims 21 and 34 are further amended to clarify that the antioxidant compositions used in the methods of the present invention contain at least two antioxidants selected from the listed antioxidants. Support for these amendments can be found in, *e.g.*, Specification page 3, lines 4-12, page 21, lines 14-25; originally-filed claim 1; and previously-presented claims 14 and 27. No new matter has been introduced by the present amendments.

Obviousness-Type Double Patenting

Claims 14-39 are rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1-12 of US Patent No. 6, 764,693. Applicant respectfully submits that a Terminal Disclaimer will be filed in the above-referenced patent application upon the determination of allowable subject matter in the instant application.

35 U.S.C. §103

1. Claims 14-23 and 27-36 are rejected under 35 U.S.C. §103(a) as being unpatentable over Halliwell (1991) Free Radicals in Biology and Medicine (hereinafter "**Halliwell**") or Packer (1992) Proc. Soc. Exper. Biol. Med (hereinafter "**Packer**") in view of U.S. Patent 5,013,556 (hereinafter "**Woodle**"), EP 0455 386 (hereinafter "**EP '386**"), and JP 62178521 (hereinafter "**JP '521**"). Applicants traverse.

Claims 14-23 and 27-36 are drawn to either a method of treating a disease or injury induced by pathological free radical reactions or a method for reducing the deleterious effects of pathological free radical reactions in a mammal exposed to a caustic gas. The claims require the administration of an amphipathic antioxidant composition. The composition requires: (i) a population of liposomes suitable for undergoing peroxidation and lysis; and (ii) at least two non-enzymatic amphipathic antioxidants. Furthermore, the claims require that the amphipathic antioxidant compositions quench free radicals and reduce the tissue damage induced by the exposure to a caustic gas.

None of **Halliwell**, **Packer**, **Woodle**, **EP '386**, or **JP '521**, either alone or in combination, bear on the patentability of new claims 14-23 and 27-36.

Halliwell and Packer

The Examiner states that **Halliwell** and **Packer** "show the involvement of free radicals in various diseases and the counter acting (sic) effects of various antioxidants against the free radicals." The Examiner admits that these two references fail to teach the administration of antioxidants in liposomes or the administration of the combination of antioxidants in the treatment of free radical induced disease conditions. November 18, 2004 Office Action at page 4. However, **Halliwell** and **Packer** are fatally deficient in teaching or even suggesting several other aspects of the present invention, as claimed herein. First, although these references may suggest the use of antioxidants in various diseases, there is no teaching or suggestions of using an antioxidant composition for reducing the damage induced by exposure to a caustic gas. Further, these references not only fail to disclose the combination of antioxidants, these references fail to disclose, teach or suggest the ***amphipathic antioxidant composition*** of the present invention. As required by the present claims, the amphipathic antioxidant composition of the present invention requires: (i) a population of liposomes suitable

for undergoing peroxidation and lysis; and (ii) at least two non-enzymatic, amphipathic antioxidants. These required claim elements are simply lacking in both **Halliwell** and **Packer**.

Halliwell and Packer in view of Woodle, EP '386, and or JP '521

None of **Woodle**, **EP '386**, or **JP '521**, either alone or in combination, help cure the deficiencies of **Halliwell** and **Packer** (if these combinations were proper, which they are not).

First, the combination of the **Halliwell** and **Packer** references with **Woodle**, **EP '386**, and/or **JP '521** is improper. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found in either the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Moreover, the prior art must suggest the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). **Halliwell** teaches the involvement of free radicals in a variety of human diseases. **Packer** teaches interactions among antioxidants in health and disease. Both references are silent on the administration of antioxidants in liposomes or the administration of the combination of antioxidants in the treatment of free radical induced disease conditions. Moreover, nothing in **Halliwell** and **Packer** would suggest the desirability of combining at least two amphipathic antioxidants with a population of liposomes suitable for undergoing peroxidation and lysis, all required elements of the present claims.

Second, even if the combination of the **Halliwell** and **Packer** references with **Woodle**, **EP '386**, and/or **JP '521** were proper (and they are not), such combination would not lead to the claimed invention.

Halliwell and Packer in view of Woodle

Woodle does not cure the deficiencies of the **Halliwell** and **Packer** references. **Woodle** is directed to increasing the circulating time of a liposome encapsulated drug and demonstrating the sustained release of liposome encapsulated drugs. There is not one word in **Woodle** regarding a liposomal formulation with two or more antioxidants. Moreover, **Woodle** is deficient in several other aspects of the present invention, as claimed herein. **Woodle** also fails to disclose (i) populations of liposomes suitable for undergoing peroxidation and lysis, (ii) amphipathic antioxidant compositions, and (iii) the use of such amphipathic antioxidant

compositions for reducing the damage induced by exposure to a caustic gas, as required by the claims of the present invention. In sum, **Woodle** simply fails to disclose, teach or even suggest a method for reducing the deleterious effects of pathological free radical reactions in a mammal exposed to a caustic gas or the compositions required to do so.

Halliwell and Packer in view of EP '386

The Examiner states that **EP '386** "teaches that the antioxidants, vitamin C and vitamin E can be encapsulated together in liposomes." The Examiner also recites that **EP '386** "further teaches the reasons for the inclusion of both vitamins C and E in the liposomes." See, November 18, 2004 Office Action at page 5.

Again, as discussed above, in addition to its failure to disclose a liposomal formulation with two or more antioxidants, **Halliwell and Packer** are deficient in several other aspects of the present invention, as claimed herein.

EP '386 does not cure the deficiencies of **Halliwell and Packer**. Like **Halliwell and Packer**, **EP '386** also fails to disclose amphipathic antioxidant compositions comprising populations of liposomes suitable for undergoing peroxidation and lysis, and the use of such for amphipathic antioxidant compositions for quenching of pathological free radical reactions, and for reducing the damage induced by the pathological free radical reactions, all required by the claims of the instant application. **EP '386** relates to fat-based food products, and particularly to a problem encountered in fat systems in cream-filled biscuits in which an additive formulated as an emulsion contains water droplets that migrate to the biscuit and adversely affect eating quality. Since **EP '386** discloses a fat-based medium with liposomes containing vitamin C and vitamin E for preventing the oxidation of fats and oils in biscuits, this reference alone, or in combination with **Halliwell and Packer**, does not disclose, teach or suggest a method of treating a disease or injury induced by exposure to a caustic gas or a method for reducing the deleterious effects of exposure to a caustic gas, as claimed in the present invention.

Halliwell and Packer in view of JP '521

The Examiner also cites, an abstract of a Japanese patent entitled "Liposome Containing Hemoglobin," as teaching the encapsulation of both vitamins C and E together in liposomes, suggesting the invention is obvious when the teachings of **JP '521** are combined

with the primary references, **Halliwell** and **Packer**. See, November 18, 2004 Office Action at page 5.

Again, as discussed above, in addition to its failure to disclose a liposomal formulation with two or more antioxidants, **Halliwell** and **Packer** are deficient in several other aspects of the present invention, as claimed herein.

JP '521 does not cure the deficiencies of **Halliwell** and **Packer**. **JP '521** is directed to the prevention of oxidation of hemoglobin and an artificial erythrocyte using an aqueous solution of hemoglobin containing vitamin C in a liposome and a membrane containing vitamin E. Like **Halliwell** and **Packer**, **JP '521** also fails to disclose amphipathic antioxidant compositions comprising populations of liposomes suitable for undergoing peroxidation and lysis, and the use of such for amphipathic antioxidant compositions for reducing the damage induced by the exposure to a caustic gas. The **JP '521** reference alone, or in combination with **Halliwell** and **Packer**, does not disclose, teach or suggest a method of treating a disease or injury induced by exposure to a caustic gas or a method for reducing the deleterious effects of exposure to a caustic gas, as claimed in the present invention.

In sum, the five references cited by the Examiner, **Halliwell**, **Packer**, **Woodle**, **EP '386**, and **JP '521**, taken alone or in combination, are fatally deficient and cannot lead the ordinarily skilled artisan to the invention, as claimed herein. For these reasons, Applicant respectfully request reconsideration and withdrawal of the 35 U.S.C. §103(a).

2. Claims 14-23 and 27-36 are also rejected under 35 U.S.C. §103(a) as being unpatentable over **Halliwell** (1991) Free Radicals in Biology and Medicine (hereinafter "**Halliwell**") or **Packer** (1992) Proc. Soc. Exper. Biol. Med (hereinafter "**Packer**") in view of U.S. Patent 5,013,556 (hereinafter "**Woodle**"), **EP 0455 386** (hereinafter "**EP '386**"), and **JP 62178521** (hereinafter "**JP '521**"), further in view of UNIMED's advertisement (hereinafter "**UNIMED**"). Applicants traverse.

The references **Halliwell**, **Packer**, **Woodle**, **EP '386**, and **JP '521** have all been discussed above.

Halliwell and Packer in view of Woodle, EP '386, and or JP '521 in further view of UNIMED

The Office Action recites that “**UNIMED**’s advertisement on **ONDROX™** shows the availability of several antioxidants in an encapsulated form for sustained release. **UNIMED** teaches that the amounts of antioxidants are theoretically synergistic (note the entire advertisement).” The Office Action also recites that **UNIMED** on the cover page “teaches the reasons for the administration of antioxidants.” See, November 18, 2004 Office Action at pages 6-7.

However, as discussed above, in addition to its failure to disclose a liposomal formulation with two or more antioxidants, **Halliwell** and **Packer** are deficient in several other aspects of the present invention, as claimed herein. There is not one word in either **Halliwell** and **Packer** regarding populations of liposomes suitable for undergoing peroxidation and lysis, amphipathic antioxidant compositions, and the use of such for amphipathic antioxidant compositions for reducing the damage induced by exposure to a caustic gas, as required by the claims of the present invention. **Halliwell** and **Packer** simply fail to disclose, teach or even suggest a the use of an amphipathic antioxidant composition for treating a disease or injury induced by exposure to a caustic gas or a method for reducing the deleterious effects of pathological free radical reactions in a mammal exposure to a caustic gas.

UNIMED does not cure the deficiencies of **Halliwell** and **Packer**. Since **ONDROX™** is directed only to a formulation for oral administration in tablet form, **UNIMED**, like **Halliwell** and **Packer**, also fails to disclose amphipathic antioxidant compositions comprising populations of liposomes suitable for undergoing peroxidation and lysis, and the use of such for amphipathic antioxidant compositions for quenching of pathological free radical reactions, and for reducing the damage induced by the pathological free radical reactions. Indeed, the description of **ONDROX™** in **UNIMED**’s advertisement clearly highlights the deficiencies of **UNIMED**. As stated in the description of **ONDROX™** provided under the section entitled: “What exactly is **ONDROX™**?”:

ONDROX™ is a multi-antioxidant nutritional supplement developed at a major university research center.

It is designed to provide a balanced range of micronutrients and anti-oxidants to individuals who wish to ensure -- or whose physicians have recommended that they make certain -- that their diets contain precise levels of these agents.

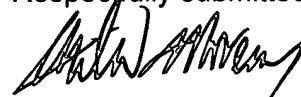
ONDROX™ is not a drug, nor is it a treatment for any disease. **ONDROX™** is a nutritional supplement... [Emphasis added.]

Since **UNIMED** clearly states that their composition is not a drug nor a treatment for any disease, this reference teaches away from the present claimed invention. A person skilled in the art would not administer a "nutritional supplement" to a mammal exposed to a caustic gas and nor would the skilled artisan expect that **UNIMED** would produce a reduction of the deleterious effects of pathological free radical reactions in a mammal exposed to a caustic gas. Accordingly, **UNIMED** alone, or in combination with **Halliwell** and **Packer**, does not disclose, teach or suggest a method of treating a disease or injury induced by pathological free radical reactions or a method for reducing the deleterious effects of pathological free radical reactions in a mammal exposed to a caustic gas, as claimed in the present invention.

CONCLUSION

On the basis of the foregoing amendments, applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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